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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Kasibhatla *et al.*

Appl. No. 10/046,548

Filed: January 16, 2002

For: **Methods of Identifying
Potentially Therapeutically
Selective and Effective Anti-
Cancer Agents that are Inducers of
Apoptosis**

Confirmation No. 1805

Art Unit: 1651

Examiner: *To be assigned*

Atty. Docket: 1735.0610001/RWE/ALS

Information Disclosure Statement

Commissioner for Patents
Washington, D.C. 20231

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. A copy of each of these documents is provided.

The Examiner's attention is directed to co-pending U.S. Patent Application No. 09/454,595 of Weber, E. *et al.*, filed December 7, 1999, and submitted herewith as AS18, which is directed to related technical subject matter.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not



be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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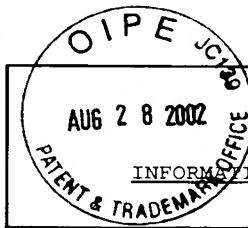
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1651

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA1	4,336,186	06/22/1982	Gargiulo et al.	260	112.5 R	02/09/1981
	AB1	4,557,862	12/10/1985	Mangel et al.	260	112 R	10/28/1983
	AC1	4,640,893	02/03/1987	Mangel et al.	435	23	09/27/1985
	AD1	5,208,148	05/04/1993	Haugland et al.	435	14	12/07/1990
	AE1	5,227,487	07/13/1993	Haugland et al.	546	15	04/16/1990
	AF1	5,362,628	11/08/1994	Haugland et al.	435	18	03/05/1993
	AG1	5,443,986	08/12/1995	Haughland et al.	435	4	07/06/1993
	AH1	5,556,992	09/17/1996	Gaboury et al.	549	227	09/02/1994
	AI1	5,576,424	11/19/1996	Mao et al.	536	17.9	11/08/1994
	AJ1	5,587,490	12/24/1996	Goodrich, Jr., et al.	549	282	12/10/1993
	AK1	5,605,809	02/25/1997	Komoriya et al.	435	23	10/28/1994

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL1	WO 93/10461	05/27/1993	WIPO			Yes No
	AM1	EP 0 285 179 B1	05/16/1993	Europe			Yes No
	AN1	CA 2,119,840	09/27/1994	Canada			Yes No
	AO1	WO 96/20721	07/11/1996	WIPO			Yes No
	AP1	WO 98/55863	06/05/1998	WIPO			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	1	Allen, R.T. et al., "Mechanisms controlling cellular suicide: role of Bcl-2 and caspases," <i>Cell. Mol. Life Sci.</i> 54:427-445, Birkhäuser Verlag (1998).
AS	1	Assfalg-Machleidt, I. et al., "Membrane Permeable Fluorogenic Rhodamine Substrates for Selective Determination of Cathepsin L," <i>Biol. Chem. Hoppe-Seyler</i> 373:433-440, Walter de Gruyter & Co. (1992).
AT	1	Biomol. Research Laboratories, Inc., "Apoptosis Inducers and the Assay of Caspase Activity," <i>FASEB J.</i> 12:A1488, Abstract No. T10, Federation of American Societies for Experimental Biology (1998).

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	AA2	5,698,411	12/16/1997	Lucas et al.	435	29	05/18/1995
	AB2	5,714,342	02/03/1998	Komoriya et al.	435	23	10/27/1995
	AC2	5,733,719	03/31/1998	Jaffe et al.	435	4	05/18/1995
	AD2	5,773,236	06/30/1998	Diwu et al.	435	15	04/25/1997
	AE2	5,776,720	07/07/1998	Jaffe et al.	435	29	05/18/1995
	AF2	5,834,216	11/10/1998	Roizman et al.	435	7.21	09/06/1995
	AG2	5,843,635	12/01/1998	Schlossman et al.	435	5	02/27/1995
	AH2	5,849,513	12/15/1998	Jaffe et al.	435	29	07/31/1997
	AI2	5,871,946	02/16/1999	Lucas et al.	435	18	05/18/1995
	AJ2	5,897,992	04/27/1999	Fearnhead et al.	435	29	09/27/1996
	AK2	5,908,750	06/01/1999	Reed, J.C. et al.	435	6	04/11/1997

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	AL2	WO 98/57664	12/23/1998	WIPO			Yes No
	AM2	WO 99/18856	04/22/1999	WIPO			Yes No
	AN2	WO 00/07017	02/10/2000	WIPO			Yes No
	AO2	WO 00/45165	08/03/2000	WIPO			Yes No
	AP2	WO 01/79187 A2	10/25/2001	WIPO			Yes No

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AR	2	Bonneau, P. et al., "Design of Fluorogenic Peptide Substrates for Human Cytomegalovirus Protease Based on Structure-Activity Relationship Studies," <i>Anal. Biochem.</i> 255:59-65, Academic Press, Inc. (1998).
AS	2	DiLanni, C.L. et al., "In Vitro Activity of the Herpes Simplex Virus Type 1 Protease with Peptide Substrates," <i>J. Biol. Chem.</i> 268:25449-25454, American Society for Biochemistry and Molecular Biology, Inc. (1993).
AT	2	Dinarello, C.A., "Interleukin-1 and Interleukin-1 Antagonism," <i>Blood</i> 77:1627-1652, The American Society of Hematology (1991).

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	AA3	5,976,822	11/02/1999	Landrum et al.	435	23	08/20/1997
	AB3	6,075,020	06/13/2000	Cincotta et al.	514	224.8	12/03/1998
	AC3	6,077,684	06/20/2000	Kravtsov	435	30	11/14/1996
	AD3	6,200,969 B1	03/13/2001	Fritz et al.	514	214	09/12/1997
	AE3	6,248,904 B1	06/19/2001	Zhang et al.	549	227	07/21/1999
	AF3	6,251,614 B1	06/26/2001	Fritz et al.	435	22	05/10/1999
	AG3	6,270,980 B1	08/07/2001	Fritz et al.	435	7.2	06/05/1997
	AH3	6,335,429 B1	01/01/2002	Cai et al.	530	402	03/08/2000
	AI3	6,342,611 B1	01/29/2002	Weber et al.	549	227	10/09/1998
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	AL3	WO 02/12545 A2	02/14/2002	WIPO			Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
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AR	3	Friesen, C. et al., "Involvement of the CD95 (APO-1/Fas) receptor/ligand system in drug-induced apoptosis in leukemia cells," <i>Nat Med.</i> 2:574-577, Nature Publishing Group (1996).
AS	3	Fulda, S. et al., "Betulinic Acid Triggers CD95 (APO-1/FAS)- and p53-independent Apoptosis via Activation of Caspases in Neuroectodermal Tumors," <i>Canc. Res.</i> 57:4956-4964, American Association for Cancer Research (1997).
AT	3	Gallop, M.A. et al., "Applications of Combinatorial Technologies to Drug Discovery. 1. Background and Peptide Combinatorial Libraries," <i>J. Med. Chem.</i> 37:1233-1251, American Chemical Society (1994).

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AR	4	Gamen, S. et al., "Doxorubicin-induced apoptosis in human T-cell leukemia is mediated by caspase-3 activation in a Fas-independent way," <i>FEBS Lett</i> 417:360-364, Elsevier Science B.V. (1997).
AS	4	Ganesh, S. et al., "Flow Cytometric Determination of Aminopeptidase Activities in Viable Cells Using Fluorogenic Rhodamine 110 Substrates," <i>Cytometry</i> 20:334-340, Wiley Liss, Inc. (1995).
AT	4	Gordon, E.M. et al., "Applications of Combinatorial Technologies to Drug Discovery. 2. Combinatorial Organic Synthesis, Library Screening Strategies, and Future Directions," <i>J. Med. Chem.</i> 37:1385-1401, American Chemical Society (1994).

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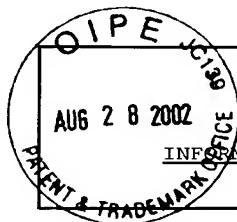
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AR	5	Hardin, J.A. et al., "A simple fluorescence method for surface antigen phenotyping of lymphocytes undergoing DNA fragmentation," <i>J. Immunol. Meth</i> 154:99-107, Elsevier Science Publishers B.V. (1992).
AS	5	Haugland, R.P. and Johnson, I.D., "Detecting Enzymes in Living Cells Using Fluorogenic Substrates," <i>J. Fluorescence</i> 3:119-127, Plenum Publishing Corporation (1993).
AT	5	Haugland, R.P., "Detecting Enzymatic Activity in Cells Using Fluorogenic Substrates," <i>Biotechnic & Histochimistry</i> 70:243-251, Williams & Wilkins (1995).

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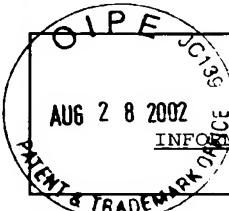
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	AL						Yes No
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	6	Haugland, R.P., <i>Handbook of Fluorescent Probes and Research Chemicals</i> , 6 th Ed., Spence, M.T.Z., ed., Molecular Probes, Inc., Eugene, Oregon. pp. 28, 54, 225-234 (1996).
AS	6	Hickman, J.A., "Apoptosis induced by anticancer drugs," <i>Cancer Metastasis Rev.</i> 11:121-139, Kluwer Academic Publishers (1992).
AT	6	Holskin, B.P. et al., "A Continuous Fluorescence-Based Assay of Human Cytomegalovirus Protease Using a Peptide Substrate," <i>Anal. Biochem.</i> 226:148-155, Academic Press, Inc. (1995).

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AR	7	Hug, H. et al., "Rhodamine 110-Linked Amino Acids and Peptides as Substrates to Measure Caspase Activity upon Apoptosis Induction in Intact Cells," <i>Biochem.</i> 38:13906-13911, American Chemical Society (1999).
AS	7	Johnson, A.F. et al., "Nonisotopic DNA Detection System Employing Elastase and a Fluorogenic Rhodamine Substrate," <i>Anal. Chem.</i> 65:2352-2359, American Chemical Society (1993)
AT	7	Jones, J. et al., "Development and Application of a GFP-FRET Intracellular Caspase Assay for Drug Screening," <i>J. Biomol. Screening</i> 5:307-317, The Society for Biomolecular Screening (October 2000).

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AR	8	Klingel, S. et al., "Flow Cytometric Determination of Cysteine and Serine Proteinase Activities in Living Cells with Rhodamine 110 Substrates," <i>Meth. Cell Biol.</i> 41:449-459, Academic Press, Inc. (1994).
AS	8	Leoni, L.M. et al., "Indanocine, a Microtubule-Binding Indanone and a Selective Inducer of Apoptosis in Multidrug-Resistant Cancer Cells," <i>J. Natl. Canc. Inst.</i> 92:217-224, Oxford University Press (February 2000).
AT	8	Leytus, S.P. et al., "New class of sensitive and selective fluorogenic substrates for serine proteinases," <i>Biochem. J.</i> 215:253-260, The Biochemical Society (1983).

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AR	9	Leytus, S.P. et al., "Rhodamine-based compounds as fluorogenic substrates for serine proteinases," <i>Biochem. J.</i> 209:299-307, The Biochemical Society (1983).
AS	9	Liang, H. and Fesik, S.W., "Three-dimensional Structures of Proteins Involved in Programmed Cell Death," <i>J. Mol. Biol.</i> 274:291-302, Academic Press, Ltd. (1997).
AT	9	Los, M. et al., "Requirement of an ICE/CED-3 protease for Fas/APO-1-mediated apoptosis," <i>Nature</i> 375:81-83, Nature Publishing Group (1995).

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AR	<u>10</u>	Los, M. et al., "Cross-Resistance of CD95- and Drug-Induced Apoptosis as a Consequence of Deficient Activation of Caspases (ICE/Ced-3 Proteases)," <i>Blood</i> 90:3118-3129. American Society of Hematology (1997).
AS	<u>10</u>	Matayoshi, E.D. et al., "Novel Fluorogenic Substrates for Assaying Retroviral Proteases by Resonance Energy Transfer," <i>Science</i> 247:954-958, American Association for the Advancement of Science (1990).
AT	<u>10</u>	Mohr, S. et al., "Macrophages resistant to endogenously generated nitric oxide-mediated apoptosis are hypersensitive to exogenously added nitric oxide donors: Dichotomous apoptotic response independent of caspase 3 and reversal by the mitogen-activated protein kinase kinase (MEK) inhibitor PD 098059," <i>Proc. Natl. Acad. Sci. USA</i> 95:5045-5050, National Academy of Sciences (1998).

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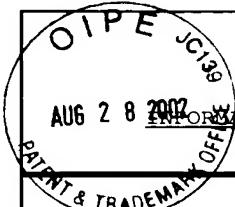
<p style="text-align: center;">O P E C 135 AUG 28 2002 INFORMATION DISCLOSURE STATEMENT</p>			ATTY. DOCKET NO. 1735.0610001/RWE/ALS		APPLICATION NO. 10/046,548		
			APPLICANT Kasibhatla et al.				
			FILING DATE January 16, 2002		GROUP 1651		
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)							
	AR	<u>12</u>	Morliere, P. et al., "Interaction of Tetrapyrrolic Rings with Rhodamine 110 and 123 and with Rhodamine 110 Derivatives Bearing A Peptidic Side Chain," <i>Biochem. Biophys. Res. Comm.</i> 146:107-113, Academic Press, Inc. (1987).				
	AS	<u>12</u>	O'Boyle, D.R. et al., "Identification of a Novel Peptide Substrate of HSV-1 Protease Using Substrate Phage Display," <i>Virology</i> 236:338-347, Academic Press, Inc. (1997).				
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January 16, 2002GROUP
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AR	<u>13</u>	Qi, X.-M. et al., "Baculovirus p35 and Z-VAD-fmk inhibit thapsigargin-induced apoptosis of breast cancer cells," <i>Oncogene</i> 15:1207-1212, Stockton Press (1997).
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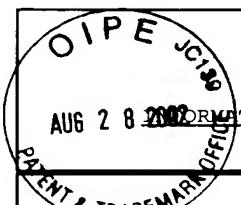
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AR	<u>14</u>	Sherr, C.J., "The Pezcoller Lecture: Cancer Cell Cycles Revisited," <i>Cancer Res.</i> 60:3689-3695, American Association for Cancer Research (July 2000).					
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AT	<u>14</u>	Tamburini, P.P. et al., "A Fluorometric Assay for HIV-Protease Activity Using High-Performance Liquid Chromatography," <i>Anal. Biochem.</i> 186:363-368, Academic Press, Inc. (1990).					
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<p style="text-align: right;">O P E SC 130</p> <p style="text-align: center;">AUG 28 2002</p> <p style="text-align: center;">INFORMATION DISCLOSURE STATEMENT</p>			ATTY. DOCKET NO. 1735.0610001/RWE/ALS		APPLICATION NO. 10/046,548	
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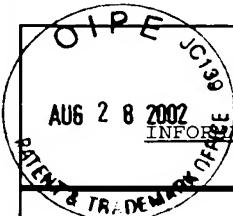
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AR	<u>15</u>	Tepper, A.D. et al., "CD95/Fas-induced Ceramide Formation Proceeds with Slow Kinetics and is not Blocked by Caspase-3/CPP32 Inhibition," <i>J. Biol. Chem.</i> 272:24308-24312, The American Society for Biochemistry and Molecular Biology, Inc. (1997).
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AT	<u>15</u>	Thornberry, N.A., "Caspases: key mediators of apoptosis," <i>Chem. Biol.</i> 5:R97-R103, Current Biology Ltd. (1998).

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AR	<u>16</u>	Toth, M.V. and Marshall, G.R., "A simple, continuous fluorometric assay for HIV protease," <i>Int. J. Peptide Protein Res.</i> 36:544-550, Munksgaard (1990).
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AR	17	Weber, J.M., "Adenovirus Endopeptidase and Its Role in Virus Infection," in: The Molecular Repertoire of Adenoviruses I. Virion Structure and Infection, Doerfler, W. and Böhm. P., eds.. Springer-Verlag, Berlin, Germany, pp.227-235 (1995).
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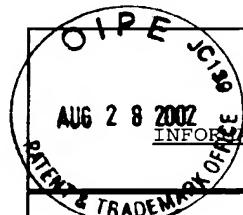
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AR	<u>18</u>	International Search Report for International Application No. PCT/US02/01018, mailed July 11, 2002.
AS	<u>18</u>	Co-pending U.S. Application No. 09/454,595, Weber, E. et al., filed December 7, 1999.
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